UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/188,051	11/06/98	SHIRLEY B	5784-25

HM22/1009

CHIRON CORPORATION
INTELLECTUAL PROPERTY DEPT.
4560 HORTON STREET
EMERYVILLE CA 94608-2916

EXAMINER	
KAM,C	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 10/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/188,051	SHIRLEY ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-48 and 85-112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-48 and 85-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 29-48 and 85-112 are pending.

Applicants' response filed on July 20, 2001 (Paper No. 21) has been fully considered, and new claims 85-112 have been added. The references in the previously submitted Information Disclosure Statement filed on April 16 and May 19, 1999 have been considered.

Rejection Withdrawn

Claim Rejections - 35 USC § 103(a)

2. The previous rejection of claims 29-48 under 35 U.S.C.103(a) as being obvious by Chang *et al.* (U.S. Patent 5,410,026), is withdrawn in view of applicants' response at pages 6-7 (Paper No. 21).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 29-48 and 85-112 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising biologically active insulin-like growth factor-1 (IGF-I) at concentration of 12 mg/ml to 200 mg/ml and at a temperature of 4 °C, a solubilizing compound of arginine, acetyl-arginine or guanidine hydrochloride, and a buffer of pH 6.0, wherein the solubilizing compound is present in the composition to make the IGF-I soluble, does not reasonably provide enablement for a composition comprising biologically active IGF-I or IGF-I analog having at least 70% sequence identity with human IGF-I at

concentration of at least 12 mg/ml and at 4 °C, a solubilizing compound comprising a guanidinium group or a solubilizing compound of an arginine analog, and a buffer of pH 5.5 or greater, wherein the solubilizing compound is present in the composition to make IGF-I or IGF-I analog soluble. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 29-48 and 85-112 encompass a composition having a pH at least 5.5 comprising biologically active IGF-I or IGF-I analog having at least 70% sequence identity with human IGF-I at concentration of at least 12 mg/ml and at 4 °C, and a solubilizing compound comprising a guanidinium group or a solubilizing compound of arginine, an arginine analog or guanidine hydrochloride (claims 29-45, 85-98 and 101-112), or a composition comprising biologically active IGF-I or IGF-I analog having at least 70% sequence identity with human IGF-I at concentration of at least 12 mg/ml in and at 4 °C, a solubilizing compound comprising a guanidinium group or a solubilizing compound of arginine, an arginine analog or guanidine hydrochloride, and a buffer of pH 5.5 or greater (claims 46-48 and 99-100), wherein the solubilizing compound is present in the composition to make IGF-I or IGF-I analog soluble. The specification, however, only discloses cursory conclusions (page 3 and lines 1-22), which state that a composition comprising biologically active IGF-I or IGF-I analog having at least 70% sequence identity with human IGF-I at concentration of at least 12 mg/ml and at 4 °C, a solubilizing compound comprising a guanidinium group or a solubilizing compound of arginine, an arginine analog or guanidine hydrochloride, and a buffer of pH 5.5 or greater, wherein the solubilizing compound is present in the composition to make IGF-I or IGF-I analog soluble.

There are no indicia that the present application enables the full scope in view of the composition of IGF-I and a solubilizing compound discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how these problems are resolved. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the scope of the claims, the amount of direction or guidance presented and the amount of experimentation necessary as discussed below.

(1). The scope of the claims

Claims 29-48 and 85-112 encompass a composition comprising biologically active IGF-I or IGF-I analog having at least 70% sequence identity with human IGF-I at concentration of at least 12 mg/ml and at 4 °C, a solubilizing compound comprising a guanidinium group or a solubilizing compound of arginine, an arginine analog or guanidine hydrochloride, and a buffer of pH 5.5 or greater, wherein the solubilizing compound is present in the composition to make IGF-I or IGF-I analog soluble. However, the specification only shows a composition comprising biologically active IGF-I at concentration of 12 mg/ml to 200 mg/ml and at 4 °C, a solubilizing compound of arginine, acetyl-arginine or guanidine hydrochloride, and a buffer of pH 6.0 wherein the solubilizing compound is present in the composition to make IGF-I soluble.

(2). The amount of direction or guidance presented and the quantity of experimentation necessary.

The specification indicates IGF-I analogs refer to biologically active derivatives or fragments of IGF-I that retain IGF-I activity and/or the ability to bind IGF receptors, which have been described in the literature (page 5, lines 27-page 7, line 18). These IGF-I analogs can have

a variety of modification in the sequence of parent IGF-I, however, the specification does not indicate which IGF-I analogs are used in the composition nor describes a composition containing a specific IGF-I analog, a solublizing compound and a buffer having a pH 5.5 to pH 9.0, wherein the solubilizing compound makes IGF-I soluble. Although the IGF-I analogs are biologically active as the parent IGF-I, there is no data indicating a solubilizing compound would enhance the solubility of the IGF-I analog to the same extent as to IGF-I. The specification does not describe a composition comprising biologically active IGF-I at concentration of at least 12 mg/ml and at 4 °C and a solubilizing compound comprising a guanidinium group in a buffer at pH other than 6.0. There is also no data indicating a solubilizing compound in the composition would make IGF-I more soluble at concentration of at least 12 mg/ml and at 4 °C in a buffer at pH other than 6.0. The specification also indicates a solubilizing compound refers to a compound containing a guanidinium group such as arginine and arginine-containing dipeptides and tripeptides (page 7, lines 19-26). However, the sequences of these peptides are not revealed, and there is no data indicating such compounds would be as soluble as arginine in the solution and can be prepared in the same range as arginine, thus enhance the solubility of IGF-I to the same extent as arginine in the composition. Therefore, it is necessary to have more guidance regarding the sequences of IGF-I analogs and the structures of arginine analogs, and to carry out further experimentation to assess the effect of the arginine analogs on the solubility of IGF-I and IGF-I analogs in the composition at a pH of 5.5-9.0.

Since it is not routine in the art to engage in *de novo* experimentation where the expectation of success is unpredictable, the skilled artisan would require additional guidance in order to make and use such composition in a manner reasonably commensurate with the scope of

the claims. Without such guidance, the experimentation left to those skilled in the art is undue because the amount of guidance is minimal regarding IGF-I analogs and arginine analogs (see above) which leads to the requirement of further experimentation to measure the solubility of the IGF-I and IGF-I analogs in the composition at pH 5.5-pH 9.0.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 29-48 and 85-112 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29-48 and 85-112 are indefinite because of the use of the term "at least about pH 5.5", "at least 70% sequence identity" and/or "at least about 12 mg". The term "at least about pH 5.5", "at least 70% sequence identity" and/or "at least about 12 mg" renders the claim indefinite; it is unclear what pH the composition has, what sequence identity the biologically active IGF-I analog has with human IGF-I, and at what concentration IGF-I or IGF-I analog is present in the composition. Claims 30-45, 47-48, 86-98, 100 and 102-112 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

3. Claims 29-48 are indefinite because of the use of the term "biologically active analogue" or "IGF-I or analogue". The term "biologically active analogue" or "IGF-I or analogue" renders the claim indefinite; it is unclear what sequence the IGF-I analog has. Claims 30-45 and 47-48

are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

4. Claims 29-45, 85-98 and 101-112 are indefinite because of the use of the term "in an amount sufficient to make IGF-I or analogue thereof soluble". The term "in an amount sufficient to make IGF-I or analogue thereof soluble" renders the claim indefinite; it is unclear what amount of a solublizing compound is needed in a composition to make IGF-I soluble. Claims 30-45, 86-98 and 102-112 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

5. Claims 31 and 46-48 are indefinite because of the use of the term "arginine analogue". The term "arginine analogue" renders the claim indefinite; it is unclear what kind of structure the arginine analogue has. Claims 47-48 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

6. Claims 31 and 46-48 are indefinite because of the use of the term "a pH of about 5.5 or greater". The term "a pH of about 5.5 or greater" renders the claim indefinite; it is unclear at what pH an arginine analogue is added in the composition. Claims 47-48 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

7. Claims 33 and 47 are indefinite because of the use of the term "at least 95% sequence identity". The term "at least 95% sequence identity" renders the claim indefinite; it is unclear what sequence identity the biologically active IGF-I analog has with human IGF-I.

8. Claims 35-39, 88-92, and 102-106 are indefinite because of the use of the term "from about.... to about...". The term "between about.... to about..." renders the claim indefinite, it is

unclear what is the range for the concentration of arginine or the pH of the composition. Use of the term "between....to.." or "about.....to about...." is suggested.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK

Patent Examiner

Christopher S. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

***

October 2, 2001